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(54) Title: **USE OF SOLASONINE**

(57) Abstract: The present invention relates to the use of the triglycoside (22R, 25R)-spiro-5-en3 β -yl- α -L-rhamnopyranosyl-(1 \rightarrow 2gal)-O-p-D-glucopyranosyl-(1 \rightarrow 3gal)- β -D-galactopyranose for the preparation of pharmaceutical compositions for treating skin tumors.

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USE OF SOLASONINE

The present invention relates to the use of the triglycoside solasonine (22R, 25R)-spiro-5-en-3 β -yl- α -L-rhamnopyranosyl-(1 \rightarrow 2gal)-O-p-D-glucopyranosyl-(1 \rightarrow 3gal)- β -D-galactopyranose for the preparation of pharmaceutical compositions for treating skin tumors.

In particular the pharmaceutical compositions according to the invention are useful for the treatment of human skin tumors, like premalignant skin lesions, malignant skin lesions, malignant skin tumors like basal cell carcinomas (BCCs), squamous cell carcinomas (SCCs), Karposi's sarcoma and benign skin tumors like actinic keratosis, keratoses and keratoacanthomas.

It is well established that certain naturally occurring conjugate solasodine glycosides have potent antineoplastic properties (WO 91/10743, Cham, B. E. and Meares H.M.(1987) Cancer Letters, 36, 111-118, Cham et al. (1991) Cancer Letters, 59, 55-58, Cham B.E. and Daunter B. (1990) Cancer Letters, 55, 221-225).

This findings however relate to the use of a crude extract of the fruits of *S. sodomaeum*, commonly referred to as BEC (Cham, B.E. and Wilson, L.(1987) Planta Medica, 53, 9-62).

BEC is incorporated in small concentrations into an over the counter (OTC) topical formulation (Curaderm®), which is used to treat skin lesions such as sunspots and keratosis.

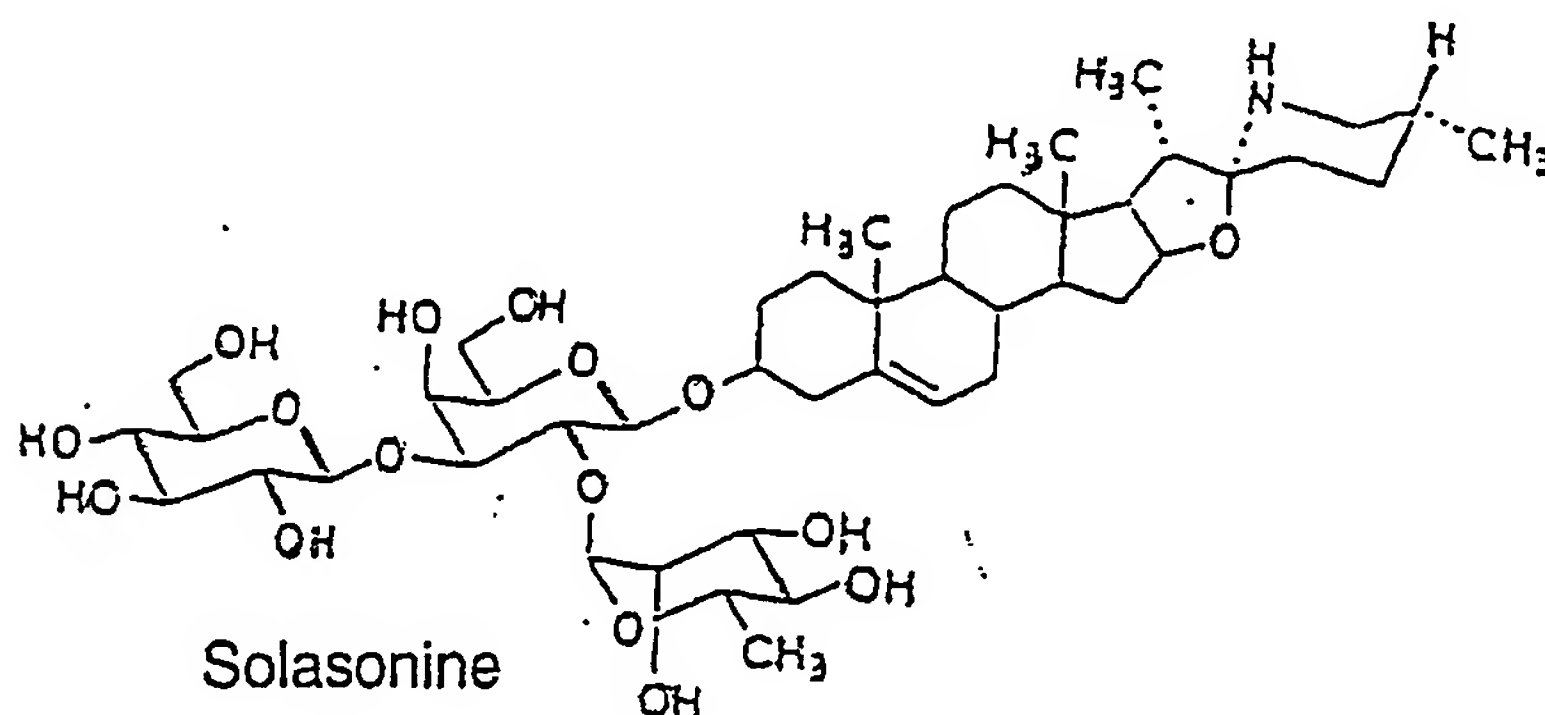
No investigations have been carried out regarding the nature of the pharmaceutical active component(s). The assumption being that all solasodine glycoside components in combination exhibit the antineoplastic effect.

Contrary to this, in accordance with the present invention it was found that the triglycoside solasonine exhibits a potent antineoplastic effect on various human skin conditions.

Detailed description of the invention

The present invention is directed to the use of the solasodine triglycoside solasonine for the preparation of pharmaceutical compositions for treating skin tumors.

Thus it has been unexpectedly found that not only the complex extract of *S. sodomaeum*, commonly referred to as BEC (Drug Future, 1988, rd 138, pages 714-716) a crude mixture of solamargine (33%), solasonine (33 %) and of an undefined fraction of di-and monoglycosides (34 %), but the individual purified *S. sodomaeum* glycoside solasonine (formula 1)



(1)

is highly effective in treating skin tumors, in particular malignant tumors such as basal cell carcinomas (BCCs), squamous cell carcinomas (SCCs) and Kaposi's sarcoma and benign tumors, like actinic keratosis, keratoses and keratoacanthomas even in the absence of the other solasodine glycoside components.

Since it is well recognized in the art that the effect of plant extract is very often caused by the often complex interactions and potentiating effects of the individual compounds present in crude plant extracts comprising more than 1 potentially active component this finding was very unexpected.

Thus the invention provides a novel, more stable, fully characterized, effective pharmaceutical composition for treating skin tumors, benign as well as malignant tumors.

The compositions of the invention may be administered e. g. orally, parenterally, topically or via an implanted reservoir or therapeutic system, whereby parenteral or topical administration are preferred. Particularly preferred is the topical administration.

Parenterally as used herein includes subcutaneous, intravenous, intramuscular, intra-articular, intrasynovial, intrasternal, intrathecal, intrahepatic, intralesional and intracranial injections or infusions. Sterile injectable compositions according to the invention may be aqueous or oleagious formulation.

These formulations may be formulated according to techniques well known in the art using suitable solvents, diluents or vehicles such as water for injection, Ringer's solution and isotonic sodium chloride solution. Optionally commonly adjuvants may also be used.

The pharmaceutical composition of the invention may also be orally administered in any orally acceptable dosage form, including capsules, tablets, granules,

suspensions or solutions, which are also formulated according techniques well known in the art.

For the particularly preferred topical administration route, the formulation may be in suitable formulations such as cremes, gels, ointments, liniments, lotions, emulsions and patches using suitable carriers and adjuvants well known in the art.

The amount of incorporated solasonine in the composition will vary depending on the particular mode of administration as well as the nature of the condition to be treated, as well as the age, weight and condition of the patient.

Preferably the compositions, especially the compositions for topical administration should be formulated to comprise between 0.001 and 10% (w/w), 0.001 and 4% (w/w)) preferably between 0.001 and 1% (w/w) and most preferably between 0.001% and 0.5% (w/w) of the formulation.

However, it should also be understood that a specific dosage and treatment regimen will depended upon variety of factors such as e. g. age, bodyweight, general state of health, sex of the patient, severity of disease and concomitant medication.

Claims

1. Use of solasonine for the preparation of a pharmaceutical composition for treating skin tumors.
2. Use according to claim 1, wherein the skin tumor is selected from premalignant skin lesions, malignant skin lesions, basal cell carcinomas (BCCs), squamous cell carcinomas (SCCs), Kaposi's sarcoma, benign skin tumors, actinic keratosis, keratoses and keratoacanthomas.
3. Use according to claim 1 or 2, wherein the composition is formulated for topical use.
4. Use according to any one of claims 1-3, wherein the concentration in the composition is between 0.001% and 10% (w/w).
5. Use according to any one of claims 1-4, wherein the concentration is between 0.001% and 4% (w/w).
6. Use according to any one of claims 1-5, wherein the concentration is between 0.001% and 1% (w/w).
7. Use according to any one of claims 1-6, wherein the concentration is between 0.001% and 0.5%.